

REMARKS

Claims 1-22 and 64-74 are pending in the application. In the Office Action mailed June 15, 2005, claims 12-21 are allowed, claims 8-10 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims, claims 1, 11, 22 and 64-74 are rejected, and claims 2-7 are withdrawn from consideration by the Examiner as belonging to non-elected species. Upon entry of the instant response, claims 1-22 and 64-74 will be pending.

Consideration of the following remarks is respectfully requested.

THE REJECTION UNDER 35 U.S.C. § 101 SHOULD BE WITHDRAWN

Claims 1, 11, and 64-74 are rejected under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter. The Examiner contends that the claims are directed to methods of “manipulating data or conversion of data without any physical transformation outside of a computer or representative of a physical activity.” The Examiner also contends that the claims are directed to non-functional descriptive material because the claims lack performance or control of a physical transformation. The Examiner further contends that the claimed methods do not have any practical utility because they do not provide at least some “physical transformation or result or representative of such physical transformation.” Applicants respectfully disagree with the Examiner’s rejection of the pending claims for the reasons presented below.

The question of whether a claim encompasses statutory subject matter should focus on the essential characteristics of the subject matter, in particular, its practical utility. *State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 U.S.P.Q.2d 1596 (Fed. Cir. 1998). Processes and systems involving transformation of data are statutory and constitute a practical application of a mathematical algorithm, formula, or calculation if they produce a useful, concrete and tangible result. *State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 U.S.P.Q.2d 1596 (Fed. Cir. 1998). A process may be patentable, irrespective of the particular form of the instrumentalities used. *Cochrane v. Deener*, 94 U.S. 780 (1876). A claim drawn to subject matter otherwise statutory does not become nonstatutory simply because it uses a mathematical formula, computer program or digital computer. *Diamond v. Diehr*, 450 U.S. 175 (1981). To determine whether a claimed process is otherwise statutory,

the proper inquiry is what the claimed method steps do, not how they are implemented. *Arrhythmia Research Technology Inc. v. Corazonix Corp.*, 22 U.S.P.Q.2d 1033 (Fed. Cir. 1992). Processes manipulating data representing physical objects or activities are statutory, if the data comprises signals corresponding to physical objects or activities external to the computer system, or if the process causes a physical transformation of the signals which are intangible representations of the physical objects or activities. Manual of Patent Examination Procedure, 8th ed., rev. 2 (May 2004) at 2100-16, citing *Arrhythmia Research Technology Inc.* “Physical transformation” is merely an example of how mathematical algorithm may bring about useful application, not an invariable requirement to constitute statutorily patentable subject matter. *AT & T Corp. v. Excel Communication Inc.* 50 U.S.P.Q.2d 1447 (Fed Cir. 1999). Claim steps employing mathematical procedures such as “converting”, “applying”, “determining”, and “comparing” are physical process steps when the steps transform one such physical, electrical signal into another. *Arrhythmia Research Technology Inc. v. Corazonix Corp.*, 22 U.S.P.Q.2d 1033 (Fed. Cir. 1992). With respect to what is not statutory, the Supreme Court identified the following three categories of subject matter that are not patentable: laws of nature, physical phenomena and abstract ideas. *Diamond v. Diehr*, 450 U.S. 175 (1981).

At the outset, Applicants respectfully submit that, irrespective of whether the methods of the rejected claims may be implemented in a computer, these methods produce useful, concrete, and tangible results, and therefore are statutory. The Examiner erred in contending that the claimed methods do not have any practical utility because they do not provide some “physical transformation or result or representative of such physical transformation.” The rejected claims are directed to methods for evaluating specificity of a drug based on a drug response profile and pathway response profiles. For example, in the method of claim 1, the activity of a drug against its target pathway (D_{target}) in a biological sample and activity of the drug against at least one of its off-target pathways ($D_{off - target}$) are respectively represented by quantities characterizing drug responses and/or pathway responses, and the specificity of the drug is evaluated by comparing D_{target} and $D_{off - target}$. In the method of claim 11, the specificity of a drug is evaluated by comparing the activity of a drug against its target pathway (D_{target}) in a biological sample and activity of said drug against at least one of its off-target pathways ($D_{off - target}$) and calculating a specificity index. In the method of claim

64, a drug response profile is decomposed into one or a combination of pathway response profiles, and the specificity of the drug is evaluated by comparing, among the one or a combination of pathway response profiles, the pathway response profiles for the one or more biological pathways associated with therapeutic effects of the drug with the pathway response profiles for the one or more biological pathways that are associated with one or more non-therapeutic effects of the drug. Thus, the methods produce information regarding important pharmaceutical properties of a drug, i.e., the specific, desired, therapeutic biological effects of the drug relative to the non-therapeutic effects, i.e., effects of the drug which are not desired and do not have a therapeutic benefit, of the drug. An assertion that such claims do not have any practical utility and do not provide useful, concrete, and tangible result is incorrect and is contradictory to the applicable case law. In *State Street Bank & Trust Co. v. Signature Financial Group Inc.*, the court held that

... the transformation of data, representing discrete dollar amounts, by a machine through a series of mathematical calculations into a final share price, constitutes a practical application of a mathematical algorithm, formula, or calculation, because it produces "a useful, concrete and tangible result"--a final share price momentarily fixed for recording and reporting purposes and even accepted and relied upon by regulatory authorities and in subsequent trades.

State Street Bank & Trust Co. v. Signature Financial Group Inc., 47 U.S.P.Q.2d 1596, 1601 (Fed. Cir. 1998). In *Arrhythmia Research Technology Inc. v. Corazonix Corp.*, regarding claims directed to a method for analyzing electrocardiograph signals to determine the presence or absence of a predetermined level of high-frequency energy in the late QRS signal, the court held that manipulation of numbers representing electrocardiograph signals related to the patient's heart function to generate an output which indicates whether the patient is at high risk for ventricular tachycardia corresponded to a useful, concrete or tangible thing -- the condition of a patient's heart, and, as such, constitutes a practical application. See *Arrhythmia Research Technology Inc. v. Corazonix Corp.*, 22 U.S.P.Q.2d 1033 (Fed. Cir. 1992). Thus, since a final share price momentarily fixed for recording and reporting purposes, and a numerical value indicating whether a patient is at high risk for ventricular tachycardia, have been determined to be useful, concrete and tangible results, the specificity of a drug, which indicates the therapeutic effects of the drug relative to the non-therapeutic effects of the drug, cannot be otherwise.

The Examiner contends that the requirement of production of a useful, concrete, and tangible result is interpreted as requiring “at least some physical transformation or result or representative of such physical transformation.” The Examiner also contends that the methods as claimed in the rejected claims are deemed per se manipulations of data without any physical transformation, i.e., allegedly the concrete or tangible requirement. Applicants first respectfully submit that it is unclear as to what the Examiner means by the phrase “at least some physical transformation or result or representative of such physical transformation.” If the Examiner means that in order to constitute a useful, concrete, and tangible result, the result cannot be a numerical value, such a contention clearly contradicts the applicable case law. As discussed above, a final share price and a numerical value indicating whether a patient is at high risk for ventricular tachycardia, have been deemed useful, concrete and tangible results. In *State Street Bank* case, the court held that “[t]his renders it statutory subject matter, even if the useful result is expressed in numbers, such as price, profit, percentage, cost, or loss.” *See State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 U.S.P.Q.2d 1596, 1602 (Fed. Cir. 1998). In *Arrhythmia* case, the court held that the fact that “the product is numerical is not a criterion of whether the claim is directed to statutory subject matter.” *See Arrhythmia Research Technology Inc. v. Corazonix Corp.*, 22 U.S.P.Q.2d 1033, 1039 (Fed. Cir. 1992). If the Examiner means that in order to constitute a useful, concrete, and tangible result, there must be some useful real-world impact, then the requirement is clearly satisfied by the presently claimed methods. As discussed above, the real-world impact of the claimed methods is the determination of the specificity of a drug, which provides information regarding the efficacy and the safety of the drug.

Applicants also respectfully submit that an interpretation of the requirement of production of a useful, concrete, and tangible result as a requirement of having “at least some physical transformation or result or representative of such physical transformation” is inconsistent with the case law. Applicants also respectfully submit that an interpretation of the requirement of production of a useful, concrete, and tangible result as a requirement of having “at least some physical transformation or result or representative of such physical transformation” is inconsistent with the case law. In *AT & T Corp. v. Excel Communication Inc.* 50 U.S.P.Q.2d 1447 (Fed Cir. 1999), the court addressed directly the requirement of “physical transformation”, and held that physical transformation is merely an example of how a mathematical algorithm may bring about useful application, not an invariable requirement.

The court held that

[t]he notion of “physical transformation” … is not an invariable requirement, but merely one example of how a mathematical algorithm may bring about a useful application. … This understanding of transformation is consistent with our earlier decision in *Arrhythmia Research Technology Inc. v. Corazonix Corp.*, 22 USPQ2d 1033 (Fed. Cir. 1992). … The *Arrhythmia* court reasoned that the method claims qualified as statutory subject matter by noting that the steps transformed physical, electrical signals from one form into another form -- a number representing a signal related to the patient's heart activity, a non-abstract output. [Citation omitted] The finding that the claimed process “transformed” data from one “form” to another simply confirmed that *Arrhythmia*'s method claims satisfied Section 101 because the mathematical algorithm included within the process was applied to produce a number which had specific meaning -- a useful, concrete, tangible result -- not a mathematical abstraction. [Citation omitted] (emphasis added)

AT & T Corp. v. Excel Communication Inc. 50 U.S.P.Q.2d 1447, 1452 (Fed Cir. 1999). *AT & T Corp. v. Excel Communication Inc.* also sets out what constitutes a useful, concrete, tangible result, i.e., a number which had specific meaning and not a mathematical abstraction.

Furthermore, Applicants respectfully submit that the rejected claims nonetheless satisfy the requirement of having “at least some physical transformation or result or representative of such physical transformation.” For example, the activity of a drug against its target pathway in a biological sample and the activity of the drug against off-target pathways in the biological sample are physical activities of the drug, the specificity of the drug is a physical attribute of the drug, and drug response profile and pathway response profiles each contains a set of physical measurements of cellular constituents. Thus, the claimed step of “comparing activity of a drug against its target pathway (D_{target}) in a biological sample and activity of said drug against at least one of its off-target pathways ($D_{\text{off-target}}$) in said biological sample” transforms quantities representing physical activities of the drug into a quantity representing a physical attribute of the drug. The claimed step of “decomposing a drug response profile into one or a combination of pathway response profiles” transforms one set of physical measurements into one or a combination of other sets of physical measurements. The holding in *Arrhythmia Research Technology Inc. v. Corazonix Corp.* is clearly applicable to the instant case. Thus, the rejected claims clearly contain subject matter that has “at least some physical transformation or result or representative of such physical transformation.”

Applicants respectfully submit that the Examiner incorrectly focuses on how the method steps may be implemented in determining whether the claims are directed to statutory subject matter. The claimed methods are statutorily patentable processes irrespective of whether the method steps are implemented experimentally or otherwise, e.g., using a computer. What constitutes a statutorily patentable process was first established by the Supreme Court in *Cochrane v. Deener*. In that case, the Supreme Court held that

[t]hat a process may be patentable, irrespective of the particular form of the instrumentalities used, cannot be disputed. If one of the steps of a process be that a certain substance is to be reduced to a powder, it may not be at all material what instrument or machinery is used to effect that object, whether a hammer, a pestle and mortar, or a mill. Either may be pointed out; but if the patent is not confined to that particular tool or machine, the use of the others would be an infringement, the general process being the same. A process is a mode of treatment of certain materials to produce a given result. It is an act, or a series of acts, performed upon the subject-matter to be transformed and reduced to a different state or thing. The process requires that certain things should be done with certain substances, and in a certain order; but the tools to be used in doing this may be of secondary consequence.

Cochrane v. Deener, 94 U.S. 780, 787 (emphasis added). Since *Cochrane*, the courts have consistently held that “the particular form of the instrumentalities” or “the tools” used in carrying out process steps do not determine if the process is statutory. For example, the Supreme Court held in *Diamond v. Diehr* that “[a] process is not unpatentable simply because it contains a law of nature or a mathematical algorithm. [citation omitted] It is now commonplace that an *application* of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection.” *Diamond v. Diehr*, 450 U.S. 175, 187 (1981) (emphasis in the original). In *State Street Bank & Trust Co. v. Signature Financial Group Inc.*, the court held that

every step-by-step process, be it electronic or chemical or mechanical, involves an algorithm in the broad sense of the term. Since Section 101 expressly includes processes as a category of inventions which may be patented and Section 100(b) further defines the word “process” as meaning “process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material,” it follows that it is no ground for holding a claim is directed to nonstatutory subject matter to say it includes or is directed to an algorithm.

State Street Bank & Trust Co. v. Signature Financial Group Inc., 47 U.S.P.Q.2d 1596, 1602 (Fed. Cir. 1998). Thus, a statutory process can include steps employing a law of nature or mathematical algorithm without becoming nonstatutory.

Consistent with such a determination of what constitutes a statutory process, the law holds that to determine whether a process is statutory, the proper inquiry is not how the method steps are performed but what these steps achieve. For example, the court held in *Arrhythmia Research Technology Inc. v. Corazonix Corp.* that “to determine whether the claimed process is otherwise statutory … we determine what the claimed steps do, independent of how they are implemented” (*Arrhythmia Research Technology Inc. v. Corazonix Corp.*, 22 U.S.P.Q.2d 1033, 1038 (Fed. Cir. 1992)).

Thus, if a claim is statutory based on what the steps do, it is not rendered nonstatutory because one or more of the steps may be carried out using a mathematical formula or a computer. For example, in *Diamond v. Diehr*, the Supreme Court held that “a claim drawn to subject matter otherwise statutory does not become nonstatutory simply because it uses a mathematical formula, computer program or digital computer.” *Diamond v. Diehr*, 450 U.S. 175, 176 (1981). In *Arrhythmia Research Technology Inc. v. Corazonix Corp.*, the Federal Circuit held that “computers came to be generally recognized as devices capable of performing or implementing process steps, or serving as components of an apparatus, without negating patentability of the process or the apparatus.” (*Arrhythmia Research Technology Inc. v. Corazonix Corp.*, 22 U.S.P.Q.2d 1033, 1036 (Fed. Cir. 1992)). The court further held that

[t]hese claimed steps of “converting”, “applying”, “determining”, and “comparing” are physical process steps that transform one physical, electrical signal into another. [T]he steps of Simson's claimed method comprise an otherwise statutory process whose mathematical procedures are applied to physical process steps.

Arrhythmia Research Technology Inc. v. Corazonix Corp., 22 U.S.P.Q.2d 1033, 1038 (Fed. Cir. 1992). Thus, when statutory subject matter is the concern, processes employing a mathematical formula, computer program or digital computer are no different from processes employing a drill or mill, a flask or test tube, or a camera or spectrometer.

In the present case, as discussed above, the steps of the rejected claims operate on drug response data and pathway response data to evaluate the specificity of a drug, which provides information regarding the efficacy and the safety of the drug. The claims are not directed to an algorithm as a procedure for solving a given type of mathematical problem. As discussed above, in *Arrhythmia Research Technology Inc. v. Corazonix Corp.*, the court held that the claimed steps of “converting”, “applying”, “determining”, and “comparing” are

physical process steps that transform one physical, electrical signal into another and the claimed method comprises an otherwise statutory process whose mathematical procedures are applied to physical process steps. In the present case, the claimed steps of “comparing” and/or “decomposing” transform quantities representing the activity of a drug against its target pathway in a biological sample and activity of the drug against at least one of its off-target pathways in the biological sample and/or drug response data and pathway response data into a measure of drug specificity. Thus, the methods of the rejected claims “comprise an otherwise statutory process whose mathematical procedures are applied to physical process steps.” The rejected claims are not directed to a law of nature, a natural phenomenon, or mere abstract ideas.

The Examiner also errs in contending that the rejected claims are directed to non-functional descriptive material because the claims lack performance or control of a physical transformation. As defined in the Manual of Patent Examination Procedure (“MPEP”), section 2106, Part IV(B)(1), 8th ed., rev. 2 (May 2004), natural phenomena, abstract ideas, or laws of nature constitute descriptive material (see MPEP, at 2100-13 and 14). In the context of computer-related inventions, descriptive material can be characterized as either functional descriptive material or nonfunctional descriptive material. *Id.* Nonfunctional descriptive material includes music, literary works and a compilation or mere arrangement of data. *Id.* Functional descriptive material consists of data structures (defined as physical or logical relationship among data elements, designed to support data manipulation functions) and computer programs which impart functionality. Functionality of descriptive material refers to functional interrelationship with the way in which computing process are performed. *Id.* In other words, functional descriptive material refers to data structures and programs that reside inside a computer and affect the operation of the computer, whereas nonfunctional descriptive material refers to data that reside inside a computer but do not affect the operation of the computer. As provided in MPEP, functional descriptive material consists of data structures and computer programs which impart functionality when employed as a computer component. *Id.* The rejected claims are not directed to merely nonfunctional descriptive material as the Examiner contends. In particular, since the rejected claims do not merely recite natural phenomena, abstract ideas, or laws of nature, they are not directed to descriptive material. The rejected claims of the present invention are directed to methods for evaluating the specificity of a drug, and provide the steps for effecting such evaluation using drug response and pathway response data. When implemented in a computer, the claims

affect the operation of the computer to perform the steps of the claims. As discussed above, the rejected claims fall into the statutory subject matter under 35 U.S.C. § 101 according to applicable case law.

Therefore, Applicants respectfully submit that the rejection of claims 1, 11, and 64-74 under 35 U.S.C. § 101 should be withdrawn.

THE REJECTION UNDER 35 U.S.C. § 102 (b) and (e)
SHOULD BE WITHDRAWN

Claims 11 and 22 are rejected under 35 U.S.C. § 102 (b) and (e) as being anticipated by Goldenberg, U.S. Patent No. 5,332,567 (“Goldenberg”). The Examiner contends that Goldenberg teaches a variety of different measurements of binding of a drug to target sites vs. non-target sites to produce a ratio of target to non-target localization, and thus, Goldenberg anticipates claim 11 and 22 of the present application. Applicants respectfully disagree with the Examiner for reasons set forth below.

A claim is anticipated under 35 U.S.C. § 102 only if each and every element and limitation as set forth in the claim is found, either expressly described or inherently present, in a single prior art reference. *Glaxo, Inc. v. Novopharm Ltd.*, 52 F.3d 1043, 1047 (Fed. Cir. 1995). There must be *no differences* between the claimed invention and the reference disclosure as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Fdn. v. Genentech, Inc.* 927 F. 2d. 1565, 1576 (Fed. Cir. 1991).

The rejected claims relates to a method for evaluating specificity of a drug comprising comparing *activity of a drug against its target pathway* (D_{target}) in a biological sample and *activity of said drug against at least one of its off-target pathways* ($D_{\text{off - target}}$) in said biological sample. In the claimed methods, D_{target} and $D_{\text{off - target}}$ are each based on measurements of a plurality of cellular constituents. The comparing step comprises calculating a specificity index (SI) according to the formula:

$$SI = \frac{n \bullet D_{\text{target}}}{\sum D_{\text{off - target}}}$$

wherein: n is the number of off-target pathways (emphasis added).

Goldenberg teaches a method of targeting a diagnostic or therapeutic agent to a location of infection by injecting a patient infected with a pathogen parenterally with an antibody conjugate which specifically binds to an accessible epitope of the pathogen or a pathogen-associated antigen accreted at the location of infection (Goldenberg, Abstract). The antibody conjugate comprises a bound diagnostic or therapeutic agent for detecting, imaging or treating the infection. Goldenberg teaches that the localization of the antibody conjugate can be assayed by various detection methods. Goldenberg teaches that by using an antibody conjugated with a therapeutic, the therapeutic is localized at the target site with an enhanced target to non-target ratio.

Applicants respectfully submit that Goldenberg does not teach *activity of a drug against its target pathway* (D_{target}) in a biological sample and *activity of said drug against at least one of its off-target pathways* ($D_{\text{off-target}}$) in said biological sample. Nor does Goldenberg teach determining the specificity of a drug by calculating a ratio of D_{target} and $D_{\text{off-target}}$. As is well known in the art, a biological pathway refers to “a collection of cellular constituents related in that each cellular constituent of the collection is influenced according to some biological mechanism by one or more other cellular constituents in the collection” (see, e.g., the specification at page 7, lines 26-29). The activity of a drug on its target pathway represents the action of the drug on such an influence network of cellular constituents of the target pathway, and the activity of the drug on one or more off-target pathways represents the action of the drug on such influence networks of cellular constituents of the one or more off-target pathways (see, e.g., the specification at page 4, lines 9-16). The activity of a drug against the target pathway and the activity of the drug against one or more off-target pathways are each based on measurements of a plurality of cellular constituents. The specificity index is a ratio of such activities that measures the specificity of the action or activity of the drug. In contrast, Goldenberg teaches a ratio of binding to a target and binding to non-targets. Applicants respectfully point out that amount of binding to a target (or to a non-target) does not teach an *activity* based on measurements of *a plurality of cellular constituents*. Goldenberg’s ratio measures the specificity of delivery of a drug to its target. Therefore, Goldenberg’s ratio of target vs. non-target binding is not the specificity determined by the methods of the rejected claims. As such, Goldenberg does not anticipate

claims 11 and 22, and the rejection of these claims under 35 U.S.C. § 102 (b) and (e) based on Goldenberg should be withdrawn.

THE OBJECTION TO CLAIMS 8-10 SHOULD BE WITHDRAWN

Claims 8-10 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Since Applicants believe that the generic claims are allowable, the objection to claim 8-10 should be withdrawn.

CLAIMS WITHDRAWN FROM CONSIDERATION AS BELONGING TO NON-ELECTED SPECIES SHOULD BE CONSIDERED

Claims 2-7 are withdrawn from consideration by the Examiner as belonging to non-elected species. Since Applicants believe that the generic claims are allowable, claims 2-7 should be considered by the Examiner. Applicants respectfully request that these claims be considered by the Examiner.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and objections and allowance of the application are respectfully requested.

Respectfully submitted,

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